| | Type | L # | Hits | Search Text | DBs | Time Stamp | Comments | Error Definition | Errors |
|---|---|---|---|---|---|---|---|---|---|
| 1 | BRS | L1 | 266 | amyloid adj fibril | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:20 | | | 0 |
| 2 | BRS | L2 | 27094 | immune adj response | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:15 | | | 0 |
| 3 | BRS | L3 | 5 | 1 same 2 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:15 | | | 0 |
| 4 | BRS | L4 | 143 | amyloid same (light adj chain) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:21 | | | 0 |
| 5 | BRS | L5 | 1 | 2 same 4 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:22 | | | 0 |
| 6 | BRS | L6 | 33 | (composition or vaccine) same 1 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:32 | | | 0 |
| 7 | BRS | L7 | 16 | 1 same (removal or remove or removing) | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:36 | | | 0 |
| 8 | BRS | L8 | 2 | 7 same 2 | USPAT; US-PGPUB; EPO; JPO; DERWENT | 2002/07/16 10:36 | | | 0 |

=> d his

(FILE 'HOME' ENTERED AT 10:39:52 ON 16 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
10:40:19 ON 16 JUL 2002
L1 7972 S AMYLOID FIBRIL
L2 338117 S IMMUNE RESPONSE
L3 8 S L1 (P) L2
L4 4 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5 2300 S AMYLOID (P) (LIGHT CHAIN)
L6 9 S L5 (P) L2
L7 5 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
L8 3 S L7 NOT L4
L9 381390 S VACCINE OR (PHARMACEUTICAL COMPOSITION)
L10 24 S L1 (P) L9
L11 10 DUPLICATE REMOVE L10 (14 DUPLICATES REMOVED)
L12 9 S L11 NOT (L4 OR L8)
L13 261 S L1 (P) REMOV?
L14 0 S L13 (P) L2

=> log y

FILE 'HOME' ENTERED AT 10:39:52 ON 16 JUL 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.21 TOTAL SESSION 0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 10:40:19 ON 16 JUL 2002

FILE 'CAPLUS' ENTERED AT 10:40:19 ON 16 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE 'BIOSIS' ENTERED AT 10:40:19 ON 16 JUL 2002


FILE 'EMBASE' ENTERED AT 10:40:19 ON 16 JUL 2002


FILE 'SCISEARCH' ENTERED AT 10:40:19 ON 16 JUL 2002


FILE 'AGRICOLA' ENTERED AT 10:40:19 ON 16 JUL 2002

=> s amyloid fibril
L1 7972 AMYLOID FIBRIL

=> s immune response
L2 338117 IMMUNE RESPONSE

=> s l1 (p) l2
L3 8 L1 (P) L2

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 4 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=> d l4 1-4 ibib abs

L4 ANSWER 1 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001654245 MEDLINE
DOCUMENT NUMBER: 21558631 PubMed ID: 11701763
TITLE: Vaccination with soluble Abeta oligomers generates toxicity-neutralizing antibodies.
AUTHOR: Lambert M P; Viola K L; Chromy B A; Chang L; Morgan T E; Yu J; Venton D L; Krafft G A; Finch C E; Klein W L
CORPORATE SOURCE: Department of Neurobiology and Physiology, Northwestern University, Evanston, IL 60208, USA.
CONTRACT NUMBER: AG 13499 (NIA)
PO1 AG13138 (NIA)
SOURCE: JOURNAL OF NEUROCHEMISTRY, (2001 Nov) 79 (3) 595-605.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011115
Last Updated on STN: 20020123
Entered Medline: 20011207

AB In recent studies of transgenic models of Alzheimer's disease (AD), it has been reported that antibodies to aged beta amyloid peptide 1-42 (Abeta(1-42)) solutions (mixtures of Abeta monomers, oligomers and ***amyloid*** ***fibrils*** ) cause conspicuous reduction of amyloid plaques and neurological improvement. In some cases, however, neurological improvement has been independent of obvious plaque reduction, and it has been suggested that immunization might neutralize soluble, non-fibrillar

forms of Abeta. It is now known that Abeta toxicity resides not only in fibrils, but also in soluble protofibrils and oligomers. The current study has investigated the ***immune*** ***response*** to low doses of Abeta(1-42) oligomers and the characteristics of the antibodies they induce. Rabbits that were injected with Abeta(1-42) solutions containing only monomers and oligomers produced antibodies that preferentially bound to assembled forms of Abeta in immunoblots and in physiological solutions. The antibodies have proven useful for assays that can detect inhibitors of oligomer formation, for immunofluorescence localization of cell-attached oligomers to receptor-like puncta, and for immunoblots that show the presence of SDS-stable oligomers in Alzheimer's brain tissue. The antibodies, moreover, were found to neutralize the toxicity of soluble oligomers in cell culture. Results support the hypothesis that immunizations of transgenic mice derive therapeutic benefit from the immuno-neutralization of soluble Abeta-derived toxins. Analogous immuno-neutralization of oligomers in humans may be a key in AD vaccines.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:753260 CAPLUS
DOCUMENT NUMBER: 131:350268
TITLE: Amyloid removal using anti-amyloid antibodies
INVENTOR(S): Solomon, Alan; Hrncic, Rudi; Wall, Jonathan S.
PATENT ASSIGNEE(S): The University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9960024 | A1 | 19991125 | WO 1999-US11200 | 19990521 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2325600 | AA | 19991125 | CA 1999-2325600 | 19990521 |
| AU 9940075 | A1 | 19991206 | AU 1999-40075 | 19990521 |
| EP 1078005 | A1 | 20010228 | EP 1999-923260 | 19990521 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002515235 | T2 | 20020528 | JP 2000-549642 | 19990521 |

PRIORITY APPLN. INFO.: US 1998-86198P P 19980521
WO 1999-US11200 W 19990521

AB The authors disclose that the cell-mediated ***immune*** ***response*** to deposits of ***amyloid*** ***fibrils*** is enhanced by the opsonizing activity of anti-amyloid antibodies. In one example, amyloid deposits were shown to resolved in mice given anti-light chain antibodies; resoln. was myeloid cell (CD18)-dependent.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 MEDLINE
ACCESSION NUMBER: 88312016 MEDLINE
DOCUMENT NUMBER: 88312016 PubMed ID: 3044707
TITLE: Neuropathology of unconventional virus infections: molecular pathology of spongiform change and amyloid plaque deposition.
AUTHOR: Masters C L; Beyreuther K
CORPORATE SOURCE: Department of Pathology, University of Western Australia, Perth.
SOURCE: CIBA FOUNDATION SYMPOSIUM, (1988) 135 24-36. Ref: 28
Journal code: 0356636. ISSN: 0300-5208.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19880927

AB To the triad of neuronal loss, gliosis and spongiform change as characteristic morphological changes associated with infection of the central nervous system, one can now add the presence of scrapie-associated filaments (SAF)/PrP rods. While the host's ***immune*** ***response*** is conspicuous by its absence, the vigorous astrocytic response is presumptive evidence of the host's ability to recognize and respond to the primary neuronal insult. We assume that the spongiform change and vacuolation of neurons are of fundamental importance in the pathogenesis of the disease, realizing that neither is specific or essential for the replication of the infectious agent. The topographical distribution of lesions is partly explained by the portal of entry and retrograde spread of the virus. The temporal progression of the lesions is more clearly determined by the host genes, best illustrated by studies of the incubation period. The molecular basis of the spongiform change is unknown but it is presumed to involve some disturbance of membrane metabolism. The recognition of PrP as a membrane glycoprotein invites proposals for its role in the development of these spongiform lesions. Extracellular amyloid occurs as plaques or congophilic angiopathy in some instances, and provides the best evidence that Alzheimer's disease (AD) is in some way related to the unconventional virus diseases. However, the protein subunit (A4) of the ***amyloid*** ***fibril*** in AD and its precursor are quite distinct from the PrP subunit which constitutes the ***amyloid*** ***fibril*** in these infectious diseases. It is still unclear whether the PrP subunit in the SAF has exactly the same composition as in the extracellular ***amyloid*** ***fibril*** . Our results suggest that only a fragment of the PrP molecule is the major constituent of the extracellular fibril. Since both PrP and A4 are derived from membrane glycoproteins, the elucidation of their normal function is likely to lead to a better understanding of the spongiform and amyloidogenic lesions in these diseases.

L4 ANSWER 4 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 80091190 EMBASE
DOCUMENT NUMBER: 1980091190
TITLE: [Pathological immunology of amyloidosis].
IMMUNOPATOLOGIA DELL'AMILOIDOSI.
AUTHOR: Clerici E.
CORPORATE SOURCE: Catt. Immunol., Univ. Studi, Milano, Italy
SOURCE: Giornale di Gerontologia, (1979) 27/9 (577-582).
CODEN: GIGEAU
COUNTRY: Italy
DOCUMENT TYPE: Journal
FILE SEGMENT: 020 Gerontology and Geriatrics
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
LANGUAGE: Italian
SUMMARY LANGUAGE: English

AB Amyloidosis has as it distinguishing feature deposits of antiparallel .beta.-pleated sheet fibrils which are responsible for the pathologic manifestations of the disease. In a group of cases the protein of the fibrils is mainly composed by light polypeptide chain and/or its amino-terminal fragment. In another group of cases the major fibril protein is of a yet unknown origin. Often, if not invariably, an immunoglobulin protein is also found in these cases. During the experimental casein amyloidosis in mice, the percentage of B-lymphocytes and the macrophages of the spleen increases, while that of T-lymphocyts significantly decreases as compared to controls. Contemporaneously to these cellular modifications, both the in vivo and in vitro ***immune*** ***response*** to foreign antigens is sharply reduced, as compared to that of the normal counterparts. It is suggested that such cellular and functional alterations are compatible with a sterile blastogenesis and with an aspecific hyperproduction of immunoglobulin light chains or immunoglobulin-related polypeptides which are either transformed or incorporated into ***amyloid*** ***fibrils*** .

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=> d his

     (FILE 'HOME' ENTERED AT 10:39:52 ON 16 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:40:19 ON 16 JUL 2002
L1          7972 S AMYLOID FIBRIL
L2        338117 S IMMUNE RESPONSE
L3             8 S L1 (P) L2
L4             4 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)

=> s amyloid (p) (light chain)
L5         2300 AMYLOID (P) (LIGHT CHAIN)

=> s l5 (p) l2
L6             9 L5 (P) L2

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L6
L7             5 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)

=> s l7 not l4
L8             3 L7 NOT L4

=> d l8 1-3 ibib abs

L8   ANSWER 1 OF 3     MEDLINE
ACCESSION NUMBER:    88003667     MEDLINE
DOCUMENT NUMBER:     88003667   PubMed ID: 3115688
TITLE:               Pulmonary immunologic features of alveolar septal
                     amyloidosis associated with multiple myeloma.
AUTHOR:              Morgan J E; McCaul D S; Rodriguez F H; Abernathy D A;
                     deShazo R D; Banks D E
CORPORATE SOURCE:    Department of Medicine, Tulane University School of
                     Medicine, New Orleans.
CONTRACT NUMBER:     CA 03389 (NCI)
                     HL 07376 (NHLBI)
SOURCE:              CHEST, (1987 Oct) 92 (4) 704-8.
                     Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         198711
ENTRY DATE:          Entered STN: 19900305
                     Last Updated on STN: 19970203
                     Entered Medline: 19871106
AB   A 74-year-old man presented with interstitial pulmonary disease which was
     proven to be alveolar septal amyloidosis by transbronchial biopsy.
     Multiple myeloma was diagnosed on the basis of monoclonal IgG-lambda
     protein in serum, monoclonal lambda   ***light***     ***chains***   in
     urine, a bone marrow plasmacytosis of 22 percent, and serum IgA and IgM
     levels less than 100 mg/dl and 50 mg/dl, respectively. Appropriate
     investigations failed to show additional sites of deposition of
       ***amyloid***  . Analysis of fluid from bronchoalveolar lavage showed an
     increase in total cells recovered, a lymphocytosis with a ratio of T
     helper over T suppressor cells greater than that in peripheral blood, the
     presence of an IgG-lambda paraprotein, and an IgG/albumin ratio greater
     than that in serum. While plasma cells could not be identified in the
     recovered cell population, cultured cells from bronchoalveolar lavage
     fluid showed increased production of IgG. These findings provide evidence
     of an ongoing pulmonary   ***immune***     ***response***   resulting in
     excess IgG-lambda protein in the pulmonary compartment, a factor which may
     contribute to the development of amyloidosis.

L8   ANSWER 2 OF 3     MEDLINE
ACCESSION NUMBER:    84291494     MEDLINE
DOCUMENT NUMBER:     84291494   PubMed ID: 6381655
TITLE:               An immunologic assessment of brain-associated IgG in senile
```

cerebral amyloidosis.
AUTHOR: Goust J M; [redacted]gum M; Powers J M
CONTRACT NUMBER: USPHS-NS-16269 (NINDS)
SOURCE: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, (1984 Sep) 43 (5) 481-8.
Journal code: 2985192R. ISSN: 0022-3069.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198409
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19980206
Entered Medline: 19840928

AB Frontal and occipital lobes were taken within four hours of death from four senile patients (77-94 years) and frozen at -70 degrees C. After thawing at room temperature, gray and white matter were separated and subjected to sequential elution at pH 7.4 and pH 2.5. The eluates were processed for isoelectric focusing on 2.5% polyacrylamide gels and stained with silver nitrate; immunoblotting was done on agarose gels and stained by immunoperoxidase for IgG and ***light*** ***chains*** . Quantitation of the amount of IgG present in neutral and acidic eluates was performed by immunonephelometry and ELISA. Only the neutral eluates contained significant amounts of IgG, which were usually polyclonal. These data indicate that IgG associated with senile cerebral ***amyloid*** are not bound to any brain or vascular component and the data do not support the occurrence of an intraparenchymal ***immune*** ***response*** .

L8 ANSWER 3 OF 3 MEDLINE
ACCESSION NUMBER: 84085526 MEDLINE
DOCUMENT NUMBER: 84085526 PubMed ID: 6360758
TITLE: Unanticipated amyloidosis in dogs infused with insulin.
AUTHOR: Albisser A M; McAdam K P; Perlman K; Carson S; Bahoric A; Williamson J R
CONTRACT NUMBER: AM20579 (NIADDK)
HL13694 (NHLBI)
SOURCE: DIABETES, (1983 Dec) 32 (12) 1092-101.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198402
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840214

AB Highly purified regular porcine insulin was given by portable insulin pumps through indwelling vena caval catheters to 17 (13 normal, and 4 pancreatectomized) dogs initially weighing 15 +/- 2 kg at rates ranging from 2 to 10 mU/min (total 17-250 mg) over time periods ranging from 37 to 252 days. During the course of the study, many of the animals lost weight and became anemic. Since these conditions persisted and weight loss progressed even after cessation of insulin infusion, as many of the dogs as possible (15 of 17) were autopsied for microscopic studies. Large amounts of ***amyloid*** were demonstrated in the liver, kidney, spleen, and/or pancreas in 55% (6/11) of normal, and in 75% (3/4) of pancreatectomized dogs. The ***amyloid*** deposits were Congo red positive, exhibited classical apple green fluorescence under polarized light, and possessed the characteristic ultrastructural features of ***amyloid*** . Massive deposits of ***amyloid*** were observed in animals receiving as little as 17 mg of insulin over a time span of 52 days. In those animals with hepatic ***amyloid*** , marked hepatomegaly was present (i.e., 1200 +/- 250, X +/- SD, versus 300 +/- 25 g for normal animals) and preterminal serum alkaline phosphatase levels were markedly elevated (434 +/- 285 versus 30 +/- 14 IU/L for animals without hepatic ***amyloid*** ). The magnitude of the hepatic ***amyloid*** deposits precludes the possibility that they represent insulin aggregates or insulin-derived products per se. No evidence of ***amyloid*** was present in any of the tissue biopsy specimens obtained prior to insulin infusion. Moreover, the possibility that this represents an ***immune*** ***response*** to the injected porcine insulin has to be viewed in light

of the fact that the amino acid sequences of dog and porcine insulins are identical. It is of particular interest that the affinity of the ***amyloid*** deposits for Congo red stain was totally abolished by prior permanganate treatment, suggesting that the ***amyloid*** was derived from serum ***amyloid*** A protein rather than from immunoglobulin ***light*** ***chains*** or insulin aggregates per se. Further evidence that the protein was of the AA-type came from the initial biochemical characterization. Gel filtration on Sephadex G100 in 6 M guanidine hydrochloride identified two small molecular weight peaks of about 13,000 and 25,000 daltons, both of which inhibited the radioimmunoassay for human AA protein. (ABSTRACT TRUNCATED AT 400 WORDS)

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     (FILE 'HOME' ENTERED AT 10:39:52 ON 16 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:40:19 ON 16 JUL 2002
L1          7972 S AMYLOID FIBRIL
L2        338117 S IMMUNE RESPONSE
L3             8 S L1 (P) L2
L4             4 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5          2300 S AMYLOID (P) (LIGHT CHAIN)
L6             9 S L5 (P) L2
L7             5 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
L8             3 S L7 NOT L4

=> s vaccine Or (pharmaceutical composition)
L9       381390 VACCINE OR (PHARMACEUTICAL COMPOSITION)

=> s l1 (p) L9
L10           24 L1 (P) L9

=> duplicate remove l10
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L10
L11           10 DUPLICATE REMOVE L10 (14 DUPLICATES REMOVED)

=> s l11 not (l4 or l8)
L12           9 L11 NOT (L4 OR L8)

=> d l12 1-9 ibib abs

L12  ANSWER 1 OF 9     MEDLINE
ACCESSION NUMBER:   2002135863     MEDLINE
DOCUMENT NUMBER:    21840729   PubMed ID: 11851323
TITLE:              Towards Alzheimer's beta-amyloid vaccination.
AUTHOR:             Frenkel D; Solomon B
CORPORATE SOURCE:   Department of Molecular Microbiology and Biotechnology,
                    Faculty of Life Sciences, Tel-Aviv University, Ramat Aviv,
                    Tel-Aviv 69978, Israel.
SOURCE:             BIOLOGICALS, (2001 Sep-Dec) 29 (3-4) 243-7.
                    Journal code: 9004494. ISSN: 1045-1056.
PUB. COUNTRY:       England: United Kingdom
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200205
ENTRY DATE:         Entered STN: 20020302
                    Last Updated on STN: 20020503
                    Entered Medline: 20020502
AB   Beta-amyloid pathology, the main hallmark of Alzheimer's disease (AD), has
     been linked to its conformational status and aggregation. We recently
     showed that site-directed monoclonal antibodies (mAbs) towards the
     N-terminal region of the human beta-amyloid peptide bind to preformed
     beta- ***amyloid*** ***fibrils*** (Abeta), leading to
     disaggregation and inhibition of their neurotoxic effect. Here we report
     the development of a novel immunization procedure to raise effective
     anti-aggregating amyloid beta-protein (AbetaP) antibodies, using as
     antigen filamentous phages displaying the only EFRH peptide found to be
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the epitope of these antibodies. Due to the high antigenicity of the phage no adjuvant is required to obtain high affinity anti-aggregating IgG antibodies in animals model, that exhibit identity to human AbetaP. Such antibodies are able to sequester peripheral AbetaP, thus avoiding passage through the blood brain barrier (BBB) and, as recently shown in a transgenic mouse model, to cross the BBB and dissolve already formed beta-amyloid plaques. To our knowledge, this is the first attempt to use as a ***vaccine*** a self-anti-aggregating epitope displayed on a phage, and this may pave the way to treat abnormal accumulation-peptide diseases, such as Alzheimer's disease or other amyloidogenic diseases. 

L12 ANSWER 2 OF 9 MEDLINE
ACCESSION NUMBER: 2001269771 MEDLINE
DOCUMENT NUMBER: 21148054 PubMed ID: 11250006
TITLE: Targeting small Abeta oligomers: the solution to an Alzheimer's disease conundrum?.
AUTHOR: Klein W L; Krafft G A; Finch C E
CORPORATE SOURCE: Northwestern University Institute for Neuroscience and Dept of Neurobiology and Physiology, Northwestern University, 2153 N Campus Drive, Evanston, IL 60208, USA.. wklein@northwestern.edu
CONTRACT NUMBER: AG-13499 (NIA)
AG-15501 (NIA)
SOURCE: TRENDS IN NEUROSCIENCES, (2001 Apr) 24 (4) 219-24. Ref: 55
Journal code: 7808616. ISSN: 0166-2236.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20020420
Entered Medline: 20010521

AB Amyloid beta (Abeta) is a small self-aggregating peptide produced at low levels by normal brain metabolism. In Alzheimer's disease (AD), self-aggregation of Abeta becomes rampant, manifested most strikingly as the ***amyloid*** ***fibrils*** of senile plaques. Because fibrils can kill neurons in culture, it has been argued that fibrils initiate the neurodegenerative cascades of AD. An emerging and different view, however, is that fibrils are not the only toxic form of Abeta, and perhaps not the neurotoxin that is most relevant to AD: small oligomers and protofibrils also have potent neurological activity. Immuno-neutralization of soluble Abeta-derived toxins might be the key to optimizing AD ***vaccines*** that are now on the horizon.

L12 ANSWER 3 OF 9 MEDLINE
ACCESSION NUMBER: 76114715 MEDLINE
DOCUMENT NUMBER: 76114715 PubMed ID: 1212427
TITLE: The effect of beta aminoproprionitrile (BAPN) on experimental amyloidosis.
AUTHOR: Schechter D; Fields M; Laufer A
SOURCE: BRITISH JOURNAL OF EXPERIMENTAL PATHOLOGY, (1975 Oct) 56 (5) 466-70.
Journal code: 0372543. ISSN: 0007-1021.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197604
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760430

AB Experimental amyloidosis was induced in mice with repeated injections of complete Freund's adjuvant (CFA) reinforced with bacterial ***vaccine*** . BAPN administered in a mixture with CFA or on its own before the injection of CFA reduced the incidence of amyloidosis. The reduction in the incidence of amyloidosis following the administration of BAPN may be due to its inhibitory effect on the oxidative deamination of amino acids, which presumably inhibit cross-linking of ***amyloid***

***fibrils*** or interfere with metabolic pathways which involve the formations of mucopolysaccharide formation. It is suggested that the defective formation of the mucopolysaccharide-amyloid protein complex inhibits amyloid deposition and induces the activity of beta glucuronidase observed in the present study. The reduced incidence of amyloidosis following BAPN adminsitration cannot be due to lysosomal enzyme degradation of the amyloid as the activity of cathepsin D and acid phosphatase is decreased during this process.

L12 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:763055 CAPLUS
DOCUMENT NUMBER: 135:313600
TITLE: Methods of investigating, diagnosing, and treating amyloidosis
INVENTOR(S): Solomon, Alan; Wall, Jonathan; Hrncic, Rudi; Schell, Maria
PATENT ASSIGNEE(S): University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001077167 | A2 | 20011018 | WO 2001-US11043 | 20010405 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002019335 | A1 | 20020214 | US 2001-825872 | 20010405 |

PRIORITY APPLN. INFO.: US 2000-194684P P 20000405
AB The present invention provides a therapeutic method for removing amyloid fibrils from a patient. The present invention also provides a transgenic animal that develops systemic AA amyloidosis within three weeks for use as a tool to investigate AA amyloidosis and to evaluate agents that may be potentially useful in preventing and treating amyloid-related disorders. Further, the present invention provides diagnostic assays for monitoring Ig light chain fibrillogenesis in real-time and for identification of the chem. nature of the protein in amyloid deposits which enables the detn. of the type of amyloidosis for therapeutic and prognostic purposes.

L12 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:900627 CAPLUS
DOCUMENT NUMBER: 134:56661
TITLE: Rhodanine derivatives and their use in inhibiting and imaging amyloids
INVENTOR(S): Augelli-Szafran, Corinne Elizabeth; Glase, Shelly Ann; Purchase, Terri Stoeber
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076988 | A1 | 20001221 | WO 2000-US15072 | 20000531 |
| W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, | | | | |

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
BR 2000011440 A 200[redacted]19 BR 2000-11440 2000[redacted]1
EP 1192144 A1 20020403 EP 2000-939472 20000531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-138545P P 19990610
WO 2000-US15072 W 20000531
OTHER SOURCE(S): MARPAT 134:56661
GI

/ Structure 1 in file .gra /

AB The invention provides a method of treating Alzheimer's disease using compds. I and their pharmaceutically acceptable salts [wherein: X = SO3H, SO2NH2, or certain derivs., tetrazolyl, SONHPh, CONH2 or certain derivs., certain NH2 derivs., kojic acid nucleus, etc.; Y = certain (un)substituted aminophenyl, aminonaphthyl, indolinyl, or 1,2,3,4-tetrahydroquinolinyl groups; n = 1-3; X1, X2 = H, C1-8 alkyl, (CH2)yZ; y = 0-4; Z = H, alkyl, cycloalkyl, perfluoroalkyl, alkenyl, (un)substituted Ph or naphthyl, OH, alkoxy, alkylthio, SO3H, CO2H or derivs., etc.]. Also provided is a method of inhibiting the aggregation of amyloid proteins using I, and a method of imaging amyloid deposits using I. Claims further include compds. I, and ***pharmaceutical*** ***compns*** . contg. I. Examples include 62 synthetic examples (approx. 40 with phys. data), and 4 bioassays. For instance, condensation of rhodanine-3-ethanesulfonic acid with 4-(n-hexylmethylamino)benzaldehyde (prepns. given) in refluxing AcOH in the presence of AcONa, activation of the resultant sulfonic acid using oxalyl chloride, and amidation with CF3CONH2 using NaH in DMF, gave title compd. II as the (Z)-isomer. In an assay for inhibition of self-seeded ***amyloid*** ***fibril*** growth, II had an IC50 of 0.3 .mu.M.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:900626 CAPLUS
DOCUMENT NUMBER: 134:56660
TITLE: Rhodanine derivatives for use in a method of inhibiting amyloid protein aggregation and imaging amyloid deposits
INVENTOR(S): Augelli-Szafran, Corinne Elizabeth; Glase, Shelly Ann; Walker, Lary Craswell; Yasunaga, Tomoyuki
PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Yamanouchi Pharmaceutical Company
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076987 | A1 | 20001221 | WO 2000-US15069 | 20000531 |

W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1192143 A1 20020403 EP 2000-938021 20000531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-138544P P 19990610
WO 2000-US15069 W 20000531
OTHER SOURCE(S): MARPAT 134:56660
GI

/ Structure 2 in file .gra /

AB The invention provides a method of treating Alzheimer's disease using compds. I and their pharmaceutically acceptable salts [wherein: X = certain (un)substituted aminophenyl, aminonaphthyl, indolinyl, or 1,2,3,4-tetrahydroquinolinyl groups; n = 1-3; X1, X2 = H, C1-8 alkyl, (CH2)yZ; y = 0-4; Z = H, alkyl, cycloalkyl, perfluoroalkyl, alkenyl, (un)substituted Ph or naphthyl, OH, alkoxy, alkylthio, SO3H, CO2H or derivs., etc.]. Also provided is a method of inhibiting the aggregation of amyloid proteins using I, and a method of imaging amyloid deposits using I. Claims further include compds. I, and ***pharmaceutical*** ***compns*** . contg. I. Examples include 71 synthetic examples and 4 bioassays. For instance, condensation of rhodanine-3-acetic acid with 4-(dibutylamino)benzaldehyde in refluxing AcOH in the presence of AcONa gave title compd. II as the (Z)-isomer. In an assay for inhibition of self-seeded ***amyloid*** ***fibril*** growth, II had an IC50 of 1.5 .mu.M.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:900612 CAPLUS
DOCUMENT NUMBER: 134:56565
TITLE: Method of inhibiting amyloid protein aggregation, treating Alzheimer's disease, and imaging amyloid deposits using isoindoline derivatives
INVENTOR(S): Augelli-Szafran, Corinne Elizabeth; Lai, Yingjie; Sakkab, Annette Theresa; Walker, Lary Craswell
PATENT ASSIGNEE(S): Warner-Lambert C., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000076969 | A1 | 20001221 | WO 2000-US15073 | 20000531 |
| W: AE, AG, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000011446 | A | 20020319 | BR 2000-11446 | 20000531 |
| EP 1192131 | A1 | 20020403 | EP 2000-938023 | 20000531 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| NO 2001005992 | A | 20020206 | NO 2001-5992 | 20011207 |

PRIORITY APPLN. INFO.: US 1999-138543P P 19990610
WO 2000-US15073 W 20000531

OTHER SOURCE(S): MARPAT 134:56565
GI

/ Structure 3 in file .gra /

AB The invention provides a method of treating Alzheimer's disease using compds. I and their pharmaceutically acceptable salts [wherein: X = (un)substituted Ph; Y = (un)substituted Ph or (un)substituted pyridyl; substituents = (0-4 per ring) alkoxy, halo, alkyl, Ph, (un)substituted carbamoyl, CO2H, CO2R1, NO2, CF3, cyano, NR1R2, tetrazole, etc.; R1, R2 = H, C1-6 alkyl]. Also provided is a method of inhibiting the aggregation of amyloid proteins using I, and a method of imaging amyloid deposits using I. Claims further include compds. I, and ***pharmaceutical*** ***compns*** . contg. I. Examples include 26 synthetic examples and 4 bioassays. For instance, title compd. II was prepd. by a sequence of: (1) imidation of 3-chloroaniline with 5-nitroisobenzofuran-1,3-dione (81%); (2) redn. of nitro to amino (99%); (3) redn. of the dione functions with

AlCl3-LiAlH4 (58%), and (4) reaction with LiN(SiMe3)2 and 2-fluorobenzoic acid in THF (23%). In an [redacted]ay for inhibition of self-seed[redacted] ***amyloid*** ***fibril*** growth, II had an IC50 of 1.1 .mu.M. A combinatorial methodol. for prepn. of I is also described.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:842238 CAPLUS
DOCUMENT NUMBER: 134:16223
TITLE: Mutant genes in familial British dementia and familial Danish dementia and their use in transgenic animals as neurodegenerative disease models
INVENTOR(S): Ghiso, Jorge; Vidal, Ruben; Frangione, Blas
PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000071671 | A2 | 20001130 | WO 2000-US14726 | 20000526 |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 2000051703 | A5 | 20001212 | AU 2000-51703 | 20000526 |

PRIORITY APPLN. INFO.: US 1999-136238P P 19990526
WO 2000-US14726 W 20000526

AB Two novel mutant amyloid precursor protein (ABriPP and ADanPP) and their amyloid peptides (ABri and ADan) assocd. with Familial British Dementia and Familial Danish Dementia, resp., are disclosed. Genetic constructs comprising DNA encoding these proteins is used to produce transgenic mammals that are useful models for neurol. diseases assocd. with amyloid deposits or amyloidosis, neurofibrillary tangles, non-neuritic plaques, neuronal degeneration and behavioral deficits such as memory or learning disabilities characteristic of dementia and other symptoms of the human diseases. These models are used for screening potential therapeutic agents and methods. Also provided is a DNA-based and immunoassays for detecting the mutations, the mutant proteins and peptides, antibodies specific for the proteins and peptides. ***Vaccines*** comprising ABriPP and ADanPP fragment are claimed. Familial British dementia (FBD), previously designated familial cerebral amyloid angiopathy-British type, is an autosomal dominant disorder of undetd. origin characterized by progressive dementia, spasticity, and cerebellar ataxia, with onset at around the fifth decade of life. Cerebral amyloid angiopathy, non-neuritic and perivascular plaques and neurofibrillary tangles are the predominant pathol. lesions. Here, the identification of a unique 4K protein subunit named ABri from isolated ***amyloid*** ***fibrils*** is identified. This highly insol. peptide is a fragment of a putative type-II single-spanning transmembrane precursor that is encoded by a novel gene, BRI, located on chromosome 13. A single-base substitution at the stop codon of this gene generates a longer open reading frame, resulting in a larger, 277-residue precursor. Release of the 34 carboxy-terminal amino acids from the mutated precursor generates the ABri amyloid subunit. The mutation creates a cutting site for the restriction enzyme XbaI, which is useful for detecting asymptomatic carriers. Antibodies against the amyloid or homologous synthetic peptides recognize both parenchymal and vascular lesions in FBD patients. A point mutation at the stop codon of BRI therefore results in the generation of the ABri peptide, which is deposited as ***amyloid*** ***fibrils*** causing neuronal disfunction and dementia. A mutation in the gene assocd. with familial danish dementia (FDD), a 10 nucleotide insertion between codon 265 and 266, was also identified.

L12 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:186701 BIOSIS
DOCUMENT NUMBER: PREV200200186701
TITLE: Vlambda germline gene repertoires in plasma cells from primary amyloidosis and normal bone marrow: Preferential

association of the 3r and 6a gene segments with amyloidosis.

AUTHOR(S): Perfetti, Vittorio (1); Casarini, Simona (1); Vignarelli, Maurizio Colli (1); Palladini, Giovanni (1); Merlini, Giampaolo

CORPORATE SOURCE: (1) Internal Medicine and Medical Oncology, IRCCS Policlinico S. Matteo, University of Pavia, Pavia Italy

SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 371a. http://www.bloodjournal.org/. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Primary systemic amyloidosis (AL) is characterized by extracellular deposition of monoclonal light chain variable region (V) fragments in forms of ***amyloid*** ***fibrils*** . A small bone marrow plasma cell clone is almost invariably the source of the light chains found in tissues. AL amyloidosis occurs only in a fraction of patients with a monoclonal component and presents some peculiar features: it is preferentially associated with lambda isotype, lambdaVI family-light chain proteins, and it has very variable organ distribution (with predominance of kidney, apprxeq40%, and heart, apprxeq30%). Analysis of Vlambda gene usage may provide insights into these features. In this report, we fulfilled criteria for gene usage analysis that included unbiased sequencing strategy and patient population, as well as information on the Vlambda repertoire of polyclonal light chains expressed by normal bone marrow plasma cells, the major source of serum Ig and still an unknown aspect. Monoclonal Vlambda regions from 55 consecutive unselected primary amyloidosis patients were isolated by an unbiased inverse-PCR sequencing strategy (Anal Biochem 239:107, 1996) and Vlambda germline gene donors identified via database search. Results from amyloidosis were compared with the Vlambda repertoire (a total of 264 sequences) expressed by plasma cells isolated from 3 normal bone marrows. Results demonstrated that: a) the lambdaIII family is the most frequently employed both in amyloidosis (47%) and in normal conditions (42%); b) despite 14 of the 30 available germline segments were used in AL, gene usage was restricted: 42% of the amyloid Vlambda regions derived from just two segments, 3r (22% of cases, lambdaIII family) and 6a (20%, lambdaVI family); c) these same two gene segments show strong association with amyloidosis when compared with their prevalence in polyclonal conditions (3r, 7.3%, P<.0009; 6a, 1.9%, P<1X10-5, chi2 test); d) 6a-light chains appeared to be frequently observed in patients with major kidney involvement (P=.013, chi2 test), whereas 3r-light chains were more evenly distributed. In conclusion, amyloid Vlambda gene usage analysis demonstrates rectriction with overusage of two gene segments and provide further support to the nephrotoxic potential of 6a-light chains (Blood 98:714, 2001). Whereas the association of 6a with amyloidosis was expected, our results identify a new amyloid-associated gene segment belonging to the lambdaIII family, 3r, whose biochemical and structural feaures should be investigated to understand the association with this disorder. The fact that just two germline genes equally contribute to approximately 40% of lambda amyloid light chains will help in designing disease-specific DNA-based ***vaccines*** as well as molecules capable of interfering with the process of amyloid deposition.

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(FILE 'HOME' ENTERED AT 10:39:52 ON 16 JUL 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:40:19 ON 16 JUL 2002

L1 7972 S AMYLOID FIBRIL
L2 338117 S IMMUNE RESPONSE
L3 8 S L1 (P) L2
L4 4 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5 2300 S AMYLOID (P) (LIGHT CHAIN)
L6 9 S L5 (P) L2
L7 5 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
L8 3 S L7 NOT L4

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L9       381390 S VACCINE OR (PHARMACEUTICAL COMPOSITION)
L10          24 S L1 (P) L9
L11          10 DUPLICATE REMOVE L10 (14 DUPLICATES REMOVED)
L12           9 S L11 NOT (L4 OR L8)

=> s l1 (p) remov?
L13         261 L1 (P) REMOV?

=> s l13 (p) l2
L14           0 L13 (P) L2

=> d his

     (FILE 'HOME' ENTERED AT 10:39:52 ON 16 JUL 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:40:19 ON 16 JUL 2002
L1          7972 S AMYLOID FIBRIL
L2        338117 S IMMUNE RESPONSE
L3             8 S L1 (P) L2
L4             4 DUPLICATE REMOVE L3 (4 DUPLICATES REMOVED)
L5          2300 S AMYLOID (P) (LIGHT CHAIN)
L6             9 S L5 (P) L2
L7             5 DUPLICATE REMOVE L6 (4 DUPLICATES REMOVED)
L8             3 S L7 NOT L4
L9        381390 S VACCINE OR (PHARMACEUTICAL COMPOSITION)
L10           24 S L1 (P) L9
L11           10 DUPLICATE REMOVE L10 (14 DUPLICATES REMOVED)
L12            9 S L11 NOT (L4 OR L8)
L13          261 S L1 (P) REMOV?
L14            0 S L13 (P) L2

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FULL ESTIMATED COST                                44.92      45.13

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